Computed Tomography Screening for Lung Cancer without a Smoking Cessation Program—Not a Cost-Effective Idea

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It is hard not to be excited by the recently reported results of the National Lung Screening Trial (NLST).[1] Although advances have been made in the surgical, radiotherapeutic, and chemotherapeutic management of lung cancer over the past several decades, the long-term survival rate for lung cancer remains very low.[2] The 20% reduction in mortality observed in this large randomized multicenter lung cancer screening study with low-dose computed tomography (CT) (20% of the usual dose) compared with chest x-ray in high-risk individuals (30 or more pack-years smokers or former smokers who had quit smoking within 15 years of study entry and currently 55–74 years of age) is definitely something to celebrate. But is population-based lung cancer screening really ready for prime time? Despite the positive NLST result, we do not yet know how optimally to define the "at-risk" population, when to start screening, what screening interval to use,[3] and for how long. Moreover, there is the issue of the cost of a population-based screening program and its cost-effectiveness compared with other lung cancer control strategies.

In an increasingly cost-constrained world, this issue has to be confronted. When breast cancer screening was first introduced, over two decades ago, there were no calls for cost-effectiveness analyses before its implementation on a population basis, but times are different now. National economies cannot continue to absorb the cost of new health technologies without a thoughtful examination of the value for money proposition. This was recognized by the International Association for the Study of Lung Cancer CT Screening Task Force which recommended that the cost-effectiveness of CT screening needed to be examined before it is implemented at the national level.[4]

The article by McMahon et al.[5] addresses the issue of cost-effectiveness using an existing Lung Cancer Policy Model which simulates lung cancer development, disease progression, detection, treatment, and survival. The lung cancer natural history parameters in the model have been calibrated against US tumor registry data on age-specific cancer incidence rates; on the distribution by size, stage, and cell types of incident lung cancers; and by lung cancer-specific survival. The model simulates symptomatic, incidental, and screen-detected benign and malignant pulmonary nodules. The sensitivity of screening CT examinations was adjusted for nodule size and location of the nodule in the chest. In the base case, nodules less than 4 mm were not followed but those between 4 and 6 mm had serial high-resolution CT scans at 9 and 24 months and those 6 to 8 mm were scheduled for CT at 6, 12, and 24 months. In sensitivity analyses, fewer high-resolution CT examinations were simulated. Nodules greater than 8 mm were biopsied. Survival was modeled as a function of treatment and underlying disease characteristics. Treatment followed National Comprehensive Cancer Network consensus guidelines in place in 2000. The model simulated the life-time histories of individuals in each of six cohorts (500,000 histories per cohort) defined by age and gender (males and females; age 50, 60, or 70

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years) and incorporated the smoking histories of the US population in 1990. A background rate of smoking cessation of 3% for current smokers was included in the model. Importantly, the effects of smoking cessation with therapy consisting of bupropion and nicotine replacement therapy were incorporated and a range of posited effects on 1-year smoking abstinence rates were explored from 1.5% (i.e., lower than the assumed baseline, on the assumption that a negative screen might make the person less likely to quit) to 4%, 8%, 16%, or 30%. Costs of diagnostic tests were estimated based on Medicare payments in 2006, and treatment costs by phase of care were incorporated from the period 1992–2003.[6] The cost per quality-adjusted life-year (QALY) gained was estimated for CT screening, smoking cessation alone, and for a combined program of CT screening and smoking cessation. A societal perspective was used in the economic analysis, and patient time and caregiver time costs were included.

As with any simulation model, the outputs and any conclusions that are drawn from them are only as good as the assumptions that are made in model development. However, in several respects, the assumptions in the McMahon model are in line with what is likely to occur in the real world if CT screening is adopted. The authors simulated annual CT screening in a broader population of smokers—both younger (age 50 years to start screening) and with less cumulative smoking history (20 pack-years)—than NLST. Unlike the NLST with its three CT examinations, McMahon et al. have modeled annual CT examination which is what clinicians would likely adopt in the absence of better guidance. However, annual low-dose CT examinations combined with diagnostic CT examinations to investigate nodules could expose the screened population to the risk of radiation-induced lung cancer. This risk has been incorporated into the model providing an estimate of one of the potential harms of a CT screening program.

The assumptions around compliance with CT screening appear more realistic in the McMahon model. In the NLST, adherence to screening was more than 90%. In the simulation, 70% of eligible individuals adhered to their screening schedule. This estimate of compliance is probably still high given the fact that there are significant challenges in reaching current smokers, among whom are those most heavily addicted. Those who have quit smoking may be more motivated to attend for screening, but getting former and current smokers into a screening program and compliant with the screening interval will undoubtedly prove to be a significant implementation challenge.

It is easy to be critical of the current model. It uses the smoking history of Americans two decades ago although smoking frequency has declined since then.[7] Treatment was simulated using guidelines in place in 2000 before the general use of positron emission tomography/CT scanning for diagnosis of solitary pulmonary nodules or staging of lung cancer and the use of many of the newer (and expensive) chemotherapy agents and molecular targeted therapies. The costs of diagnostic procedures were based on Medicare reimbursement levels and are lower and probably in some cases much lower than the prices that would be charged to private payers. Treatment costs were based on patterns of care and costs of treatment in the 1992–2003 timeframe. Nonetheless, several key messages can be derived from the microsimulation model that should influence the thinking of those proposing population-based screening programs.

McMahon et al. implicitly assume that the benefits of CT screening as demonstrated in NLST can be extended to a younger age group than was included in NLST and that annual screening of persons with even a 20 pack-year smoking history has the potential to reduce lung cancer-specific mortality. These assumptions will need evidentiary support before population-based CT screening eligibility is broadened. The model projects a reduction of 18 to 25% at 10 years at a cost of $126,000 to $269,000/QALY. When radiation-induced lung cancer is included, the mortality reductions are smaller and the costs higher. Restricting screening to higher risk individuals with at least 40 pack-years and annual screening with perfect adherence yields improved cost-effectiveness ratios in the range of $110,000 to $166,000/QALY. With a 70% adherence rate, the incremental cost-effectiveness ratio compared with no screening is $280,000/QALY. The authors do not comment on whether they see such a high cost-effectiveness ratio as a barrier to the adoption of CT screening. Certainly, in comparison to the overused and out-of-date cost-effectiveness ratio of $50,000/QALY commonly applied in the context of new drug approvals, the cost/QALY of CT screening is very high. In comparison to both breast and colorectal screening with cost-effective ratios of $47,700/QALY (2006$) and $13,000 to $32,000/QALY, respectively, lung cancer screening is much less cost-effective despite having the advantage of being able to focus on individuals at higher risk of disease.[8,9]

However, the most important message of this article is not included in its title. Smoking cessation alone is substantially more cost-effective than CT screening alone and is more cost-effective than smoking cessation combined with CT screening albeit with greater benefits. The model predicts that in a cohort of 50-year-olds, if the smoking cessation rate doubled to 6% from a background rate of 3%, it would cost $17,700 to 20,800/QALY for men and women, respectively. If smoking cessation is combined with annual screening, it would also be more cost-effective for men ($73,000/QALY) and women ($40,000/QALY) than CT screening alone. That smoking cessation is far more cost-effective than CT screening either alone or in combination has very important implications for how screening programs are organized in the future. Clearly, no CT screening program should be mounted without being tightly linked to a smoking cessation program. A focus on the technology alone (low-dose CT screening) without seizing the opportunity to modify the behavior of smokers who enter the program will result in a program that has less impact on mortality reduction and one that is less cost-effective. Furthermore, the model demonstrates that if the introduction of lung CT screening programs were to result in current smokers believing that screening absolves them of the need to stop smoking, the overall effect could be very adverse.

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